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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,502	12/23/2005	Scott Eugene Conner	2947.1009-005	8241

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EXAMINER	
NOLAN, JASON MICHAEL	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
05/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,502	CONNER ET AL.	
	Examiner	Art Unit	
	JASON M. NOLAN	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-7,9-11,19,20,28,29,39,46,50,53-55,101 and 108* is/are pending in the application.

4a) Of the above claim(s) *5,19,20,28,29,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6,7,9-11,50,53-55 and 101* is/are rejected.

7)☒ Claim(s) *46 and 108* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/06/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicants Response to Election/Restriction, filed **02/28/2008**. **Claims 4-7, 9-11, 19, 20, 28, 29, 39, 46, 50, 53-55, 101, & 108** are pending in the instant application; of which **Claims 4, 5, 46, 50, & 101** are currently amended. **Claims 1-3, 8, 12-18, 21-27, 30-37, 40-45, 47-49, 51, 52, 56-100, 102-107, 109, & 114** are canceled.

Response to Restriction

Applicants' election with traverse of **Group 14** is acknowledged. Applicants point out that the elected group reads on **Claims 4, 6, 7, 9-11, 20, 46, 50, 53-55, 101, & 108**. The Examiner confirms this. Applicants' traversal alleges that the compound of Rami *et al.* does not intercept the special technical feature of the instant claims, as currently amended. The argument is moot in light of the instantly cited prior art, which shows that the common core of the instant application is not a special technical feature over the prior art, even in light of the currently amendments. For this reason, the Lack of Unity Restriction Requirement is maintained. Inasmuch, **Claims 5, 19, 20, 28, 29, 38, & 39** are withdrawn from further consideration as being drawn to non-elected inventions. Further, **Claims 4, 46, & 101** contain non-elected subject matter and are objected to herein.

Information Disclosure Statement

Applicants' information disclosure statement (IDS), filed on **07/06/2005** has been considered. Please refer to Applicants' copy of the 1449 submitted herein.

Claim Rejections - 35 USC § 102

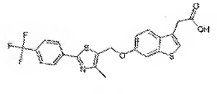
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 4, 6, 7, 9-11, 50, & 53-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng *et al.* (WO 03/074051 A1, filed 03/03/**2003**, with benefit of US Provisional 60/362,411, filed **03/07/2002**; *see* IDS). Disclosed in the publication is the compound on page 99: Example 23, shown below, wherein **Z4** = S; **Y** = bond; **E** = C(**R3**)(**R4**)-**A**, **R3 & R4** = H, **A** = carboxyl; **X** = O; **U** = CH_2 (C_1 aliphatic linker); **T1** = thiazole (**Z5** = S); **R1** = CH_3; **R2** = bond; and **R33** = phenyl, substituted by **R10** = C1 haloalkyl.

Example 23

Synthesis of [6-[4-methyl-2-(4-trifluoromethyl-phenyl)-thiazol-5-ylmethoxy]-benzo[b]thiophen-3-yl]-acetic acid (compound 23)



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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 & 101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of the formula shown in **Claim 4**, including stereoisomers and pharmaceutically acceptable salts thereof; the specification is not enabled for *solvates* thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The Nature of the Invention

The nature of the invention is the compounds and compositions of the formula shown in **Claim 4**, including all stereoisomers, pharmaceutically acceptable salts, solvates, and hydrates thereof.

The state of the prior art and the predictability or lack thereof in the art

Active pharmaceutical ingredients (APIs) are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact and generally stable format to store an API or a drug product. Understanding and controlling the solid-state chemistry of APIs, both as pure

drug substances and in formulated products, is therefore an important aspect of the drug development process. APIs can exist in a variety of distinct solid forms, including polymorphs, *solvates*, hydrates, salts, co-crystals and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms such as polymorphs and *solvates* are not so common as to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them and evaluate their properties as valuable new pharmaceutical materials. A large number of factors can influence crystal nucleation and growth during this process, including the composition of the crystallization medium and the processes used to generate super-saturation and promote crystallization, (Morissette *et al.* Advanced Drug Delivery Reviews **2004**, *56*, 275-300).

Therefore, for these reasons, the state of the prior art with respect to making solvates of biologically active compounds is one of unpredictability; since it can only be known that the compound will form a solvate when in fact it is actually formed.

Amount of direction/guidance & presence or absence of working examples

The direction or guidance present in the instant specification for the preparation of solvates of the compounds of the instant invention is lacking. There are no working examples present in the disclosure, nor is there guidance in lieu of this shortcoming. Therefore, one of skill in the art would be required to identify the correct solvent system and solvate-forming technique for each compound and, further, identify the similarities and differences between the solvates and corresponding compounds in order to determine what is useful for the modulation of a peroxisome proliferator activated receptor.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any solvate for a compound of the instant invention.

The quantity of experimentation necessary

While the level of the skill in the pharmaceutical arts is high, it would require undue experimentation of one of ordinary skill in the art to prepare any solvates for a compound of the formula as instantly claimed in **Claim 4**. The science of forming solvates is unpredictable: it can only be shown that a compound will form a solvate after it has been formed. Without guidance or working examples for solvates in the specification, the claims lack enablement. It is unknown which solvents would be useful

for forming solvates of the instant compounds. This is distinct from hydrates, for example, which form from water (solvent). This rejection can be overcome by deletion of the words "solvates" from the Claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 50 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "modulating" in **Claim 50** is a relative term which renders the claim indefinite. The term "modulating" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant application, does modulate mean that the compounds inhibit PPAR or activate PPAR? Does it mean that the compounds act as agonists or antagonists? A more descriptive term is needed; or Examiner suggests cancelling the claim.

Claim Objections

Claims 4, 46, & 101 are objected to for containing non-elected subject matter, (there are several species wherein either **Z4** is not S (benzothiophene) or **T1** is not the elected group (thiazole). Appropriate correction is required.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is **Jason.Nolan@uspto.gov**. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^{c}Kane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jason M. Nolan, Ph.D./

Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626